Remarks:

Applicant has carefully studied the final Examiner's Action mailed August 14, 2008. Applicant thanks the Examiner for their careful attention in reviewing the application. The amendments appearing above and these explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is now believed to be in condition for allowance.

Applicant responds to the outstanding Action by centered headings that correspond to the centered headings employed by the Office, to ensure full response on the merits to each finding of the Office.

Status of the Claims

Claims 1-2, 4, 7, 10, 12-17 and 19 were pending in the Office Action mail dated August 14, 2008. No claims have been amended, canceled or withdrawn. Therefore, claims 1-2, 4, 7, 10, 12-17 and 19 are currently pending and under examination.

Withdrawn Rejections and Objections

The Examiner has indicated that the rejection under 35 U.S.C. 112, second paragraph has been withdrawn in light of amendments which clarify the scope of the claims. Applicant thanks the Examiner for their consideration and withdrawal of the rejection.

Claim Rejections – 35 U.S.C. §103(a)

<u>The '832 Patent in view of Sanberg and Grabowski:</u>

Claims 1, 2, 4, and 17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,851,832 to Weiss (the '832 patent) in view of Sanberg et al. (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9) and Grabowski (1994. Exp Neural. 127(1):126-136). Applicant respectfully traverses this rejection on the grounds that (1) one or more elements are missing from the cited combination and (2) that the cited art, in combination with state of the art and the knowledge of one of ordinary skill in the art at the time of the invention, would not have imbued one of ordinary skill in the art with a reasonable expectation of success.

In rejecting claims under 35 U.S.C. § 103(a), it is incumbent upon the Office to establish a factual basis to support the legal conclusion of obviousness.[1] In so doing, the Examiner must make the factual determination set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). In Graham the court held that the obviousness analysis is based upon several factual inquiries: "[(1)] the scope and content of the prior art are to be determined; [(2)] differences between the prior art and the claims at issue are to be ascertained; and [(3)] the level of ordinary skill in the pertinent art resolved."[2] "[T]he Examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability."[3] "All words in a claim must be considered in judging the patentability of that claim against the prior art."[4] Furthermore, " '[t]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness'..."[5]

<u>One or more elements for a *prima facie* case of obviousness missing</u>

The combined references fail to establish a *prima facie* case of obviousness as outlined by MPEP 2142 for reasons including that the combined references fail to teach or suggest all claim limitations (see also MPEP 2143.03). In particular, the '832 patent does not teach or suggest (1) the administration of at least 6 million viable hNT neuronal cells nor does it teach (2) a method of treating stroke in a human, despite assertions to the contrary, and these shortcomings are not redeemed through the combination of the '832 patent with Sanberg et al. and Grabowski et al.

The Office rejects claims 1, 2, 4, and 17 under 35 U.S.C. 103(a) as being unpatentable using U.S. Patent 5,851,832 to Weiss (the '832 patent) as the primary reference. The claims at issue, as represented by claim 1, are directed to "[a] method of treating stroke in a human who has undergone a stroke at least three hours earlier, said method comprising delivering at least 6 million viable hNT neuronal cells to a plurality of brain area sites involved in the stroke." On page 7 of the Office Action dated December 29, 2005 the Office states:

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1 *In re Fine*, 837 F.2d 1071, 1073 (Fed. Cir. 1988).
2 *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). *See also KSR Int'l v. Teleflex Inc.*, 127 S.Ct. at 1734.
3 *In re Oetiker*, 977 F.2d. 1443, 1445 (Fed. Cir. 1992).
4 See MPEP 2143.03 – All Claim limitations Must be Considered – *citing in re Wilson* " 'All words in a claim must be considered in judging the patentability of that claim against the prior art.' *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)."
5 *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007) quoting In reKahn, 441 F. 3d. 977, 988 (Fed. Cir. 2006).

> As disclosed by the '832 patent, treatment of neurodegenerative disease using progeny of human neural stem cells involves first having the patient undergo a CT scan to determine the coordinates of the region to receive the transplant, then using injection cannula to inject the tissue suspension to the correct coordinates (column 42, example 14). And in an animal model of stroke precipitated by occlusion of the carotid arteries, the '832 patent discloses that neural stem cells are implanted in the lesioned areas. Also, in the actual transplantation procedure, it is taught that burr holes are drilled in the skull to allow access for cannula and injection syringes (column 62, lines 33-35), thus meeting a limitation of claim 2.
>
> The '832 patent teaches that live neural stem cells prepared for transplantation are resuspended to a cell density of 1.5×10^6 cells/ml (column 62, lines 16-22), and 1-3 µl are administered in an animal model for transplantation (column 62, lines 38-40), which would be approximately 1500-4500 cells. However, the '832 patent is silent as to the timing of the administration of neuronal cells in relation to the stroke.

First, Example 14 is directed to the "Treatment of Neurodegenerative Disease Using Progeny of Human Neural Stem Cells Proliferated In Vitro" as indicated at column 42, lines 32-34. Thus, the example is concerned with the treatment of neurodegenerative diseases, not other diseases. At column 3, lines 7-21 of the '832 patent it is provided.

> CNS disorders encompass numerous afflictions such as ***neurodegenerative diseases*** (e.g. Alzheimer's and Parkinson's), ***acute brain injury*** (e.g. **stroke**, head injury, cerebral palsy) and a large number of CNS dysfunctions (e.g. depression, epilepsy, and schizophrenia). In recent years neurodegenerative disease has become an important concern due to the expanding elderly population which is at greatest risk for these disorders. These diseases, which include Alzheimer's Disease, Multiple Sclerosis (MS), Huntington's Disease, Amyotrophic Lateral Sclerosis, and Parkinson's Disease, have been linked to the degeneration of neural cells in particular locations of the CNS, leading to the inability of these cells or the brain region to carry out their intended function. (emphasis added)

Thus, stroke is considered by the inventor's to be an acute brain injury, not a neurodegenerative disease, which is consistent with usage of the term in the art. Thus, the example is not contemplated by the inventors of the '832 patent for the treatment of stroke. Had those inventors intended to address both acute brain injury and neurodegenerative disorders, they could have captured both under the penumbra of "CNS disorders". One can only presume that they chose not to do so as evidenced by the language excerpted immediately above.

To further put Example 14 in context, an excerpt, corresponding to column 42, lines 46-60, is provided below:

> The patient undergoes CT scanning to establish the coordinates of the region to receive the transplant. The injection cannula consists of a 17-gauge stainless steel outer cannula with a 19-gauge inner stylet. This is inserted into the brain to the correct coordinates, then removed and replaced with a 19-gauge infusion cannula that has been preloaded with 30 µl of tissue suspension. The cells are slowly infused at a rate of 3 µl/min as the cannula is withdrawn. Multiple stereotactic needle passes are made throughout the area of interest, approximately 4 mm apart. The patient is examined by CT scan postoperatively for hemorrhage or edema. Neurological evaluations are performed at various post-operative intervals, as well as PET scans to determine metabolic activity of the implanted cells.

A reading of this excerpt shows this to be a prophetic example and not based upon actual treatment. Furthermore, the prophetic example is directed to the treatment, not of stroke, but of neurodegenerative diseases, which can be fairly heterogeneous in nature and extent. From such a prophetic example directed to a heterogeneous collection of diseases (not including stroke), it cannot be fairly said that one could reasonable extrapolate to the treatment of stroke, especially given the unpredictablility that accompanies any prophetic example in the bioscience treatment realm.

Additionally, with respect to the number of cells recited in the claim and the numbers cited by the Office, some observations can be made. First, it is indicated above that 3 μl/min are administered. However, no concentration is provided, so it cannot be said how many cells are administered based upon the prophetic example. Additionally, it cannot be said what disease/condition is being treated. The example is directed towards treating a "neurodegenerative disease" without specifying which disease.

To resolve the shortcoming as to the teaching of the number of administered cells the Office states that "[t]he '832 patent teaches that live neural stem cells prepared for transplantation are resuspended to a cell density of 1.5×10^6 cells/ml (column 62, lines 16-22), and 1-3 μl are administered in an animal model for transplantation (column 62, lines 38-40), which would be approximately 1500-4500 cells."[6]

It is noted that Example 14 indicates that the cannula is loaded with 30 μl and that in the Example 45, while 4-5 μl are loaded, only 1-3 μl are delivered[7] (i.e only about 2/3 of the loaded volume is delivered). Thus, assuming as the Office does in the veracity of the prophetic example in combination with the teaching of example 45, one would be motivated to treat an unspecified neurodegenerative disease by administering, at most, 45,000 cells (i.e. 4,500 cells x 30 μl loaded in the human example/3 μl delivered in the mouse) and more likely about 30,000 cells.

The Office provides their own estimates to fill in the shortcomings as to the teachings of the number of cells to be administered. On page 8 of the Office Action dated 29 December 2005 it is stated:

> It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the ***method of treating neurodegenerative disease*** taught by the '832 patent by administering a larger number of neuronal cells, as taught by Sanberg et al., after a period of at least 3 months, as taught by Grabowski et al. One of ordinary skill in the art would be motivated to do so because

[6] See Office Action dated 29 December 2005 at page 7.
[7] U.S. Patent No. 5,851,832 to Weiss et al. at column 62, lines 34-39.

> Sanberg et al. teaches a dose-dependent behavioral recovery in ischemic rats when transplanting greater numbers of hNT cells. The human brain is reported to have approximately 100 billion neurons, and one of ordinary skill in the art would estimate that the rat brain would have far fewer neurons due to its being proportionately smaller (when body size is adjusted for) and because the rat brain has far less surface area (indicated by the lack of convolutions on brain surface). If ischemic damage of equal intensity were to occur in comparably-sized brain regions in a rat and a human (again, adjusted for body size), it would be reasonable to predict that the number of neurons affected in the human would exceed the number of affected neurons in the rat. Therefore, it is also reasonable to contemplate using a greater number of neuronal cells to treat damage caused by a stroke in a human than to treat damage caused by ischemia in a rat.

Similar calculations are provided on page 4 of the Office Action dated 23 November 2007 where it was stated:

> It would have been obvious to one of ordinary skill in the art to modify the teachings of Weiss ('832 patent), who indicates that degenerative conditions such as stroke in humans can be treated by administering neural cells, by administering at least 6 million hNT cells, given the teachings of Sanberg. The motivation to do so would be to effectively treat stroke. Sanberg teaches that hNT cells are effective in ameliorating the motor effects of stroke, which is on point to claim 1, and teaches that 40,000 cells are effective. Given that an adult rat weighs approximately *0.3* kg and an adult human weighs approximately 75 kg, it would have been obvious to one of ordinary skill in the art to scale up the dose of cells used by Sanberg accordingly, thereby arriving at a dose of 10 million cells, which meets the limitation "at least 6 million cells" recited in claims 1 and 17.

First, the Office expressly recognizes that it is neurodegenerative disease that is being treated in the '832 teaching relied upon by the Office and not stroke. Second, the Office is making many assumptions in arriving at the number of cells to be administered. One of the most critical, and erroneous, assumptions made by the Office is that the size of the ischemic damage resulting from experimentally induced ischemic stroke would be mouse would be proportionally related to its body weight vis-à-vis the human. This is not the case. In fact, "rodent models of cell death in stroke produce very large infarcts that may not model the most common, and treatable, human strokes."[8] Moreover, "unlike rat MCAo, MCAo in the mouse is uniquely plagued by substantial variations in the volume of damage within and between strains and by the easy possibility generating large infarcts in widespread and diverse brain structures."[9]

Another concern is that the Office is comparing apples and oranges without recognizing it as such. The '832 patent referred to a mouse model of neurodegenerative disease. In contrast, Sanberg utilized a rat model of MCAo. It is unclear how the results of Sanberg can be extrapolated to the results of the '832 patent regarding the number of cells to be administered.

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[8] Carmichael, S. T., "Rodent Models of Focal Stroke: Size, Mechanism and Purpose", *NeuroRX: The Journal of the American Society for Experimental NeuroTherapeutics*, 2:396-409 at 398.
[9] *Id.*

The Office is also advocating varying too many variables at once (i.e. the disease to be treated, the number of bore holes, the number of cells to be administered, etc.) to chalk this up to a "mere" optimization of a parameter.

Lastly, there is no reason to conclude, and the Office offers no evidence, that the number of cells affected as a result of ischemic injury would be proportionately related to the weight of the human/animal in question. Moreover, the Office's calculations based upon weight differ from the calculations that would be achieved through a combination of Examples 14 and 45 of the '832 patent. While Applicant is not expressing an opinion about which of the two calculations may be more relevant, it merely highlights the attendant uncertainty in the number of cells to be administered. It should also be noted that the Office, in the excerpt above, states, "It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of treating neurodegenerative disease taught by the '832 patent by administering a larger number of neuronal cells ... [because] [i]f ischemic damage of equal intensity were to occur in comparably-sized brain regions in a rat and a human (again, adjusted for body size), it would be reasonable to predict that the number of neurons affected in the human would exceed the number of affected neurons in the rat." However, the '832 patent used a mouse model and not a rat model. Significant differences can exist between rat and mouse models of ischemic injury[10], so one must consider where the model results were derived before drawing conclusions.

<u>There would be no reasonable expectation of success</u>

A *prima facie* case of obviousness requires that there is a reasonable expectation of success in making the claimed invention based upon the combination and/or modification of the cited prior art.[11] Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made.[12]

"For a prior-art reference, or a combination of references, to render a claimed invention obvious, one of ordinary skill in the art at the time the invention was made must have expected a

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[10] Carmichael, S. T., "Rodent Models of Focal Stroke: Size, Mechanism and Purpose", *NeuroRX: The Journal of the American Society for Experimental NeuroTherapeutics*, 2:396-409 at 398.
[11] *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See also MPEP 2143.02 – Reasonable Expectation of Success.

reasonable chance of success in applying the teachings of the references to arrive at the claimed invention."[13] "While absolute certainty is not necessary to establish a reasonable expectation of success, there can be little better evidence negating an expectation of success than actual reports of failure." [14]

Numerous sources recount the difficulties in translating success in rodent models of stroke to meaningful clinical treatments. For example, Cheng, Y.D. et al. ("Cheng") reports that "[n]umerous agents have been found to reduce infarct size in rodent, rabbit and primate stroke models. However, the translation of neuroprotective benefits from the laboratory to the emergency room has not been successful."[15] Cheng further analyzes some of the difficulties in moving treatments from "bench-top to bedside". First in the limited factors cited by Cheng is the problem of outcome measures. Cheng states, "While most of animal stroke models used in preclinical neuroprotection studies are MCA occlusion models, patients enrolled into clinical trials often include infarcts of diverse brain regions. Thus, some animal models may be poor predictors of clinical trial results. Another factor that may play a role in the discrepancies between preclinical and clinical study outcomes is the difference in the composition of brain between rodents and humans."[16]

In a similar vein, Kleim, J.A. et al. ("Kleim") states, "It is important to recognize the limitations of rat models for informing clinical research. First, animal models of stroke will never approach the complexity of the human condition and the heterogeneity of the stroke population. … Second, the nature of the damage in human patients can differ substantially from the damage experimentally induced in laboratory rats. … Third, the degree of impairment between human stroke victims and rats is also different. … Indeed, animal studies may produce unrealistically favorable results …"[17] Kleim later concludes, "Both basic and clinical scientists must also bear in mind that animal models of stroke are not designed to mirror the human condition nor provide

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[12] *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986).
[13] PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360, 83 U.S.P.Q.2d 1289, 1301–02 (Fed. Cir. 2007), cert. denied, 2008 WL 102402 (U.S. 2008).
[14] Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp. 320 F.3d 1339, 1354 (C.A.Fed. (N.J.),2003) citing *In re O'Farrell,* 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed.Cir.1988) and *In re Rinehart,* 531 F.2d 1048, 1053-54, 189 USPQ 143, 148-49 (CCPA 1976).
[15] Cheng, Y.D. et al. " Neuroprotection for Ischemic Stroke: Two Decades of Success and Failure" *NeuroRX: The Journal of the American Society for Experimental NeuroTherapeutics*, (2004) 1:36-45 at 36.
[16] Cheng, Y.D. et al. " Neuroprotection for Ischemic Stroke: Two Decades of Success and Failure" *NeuroRX: The Journal of the American Society for Experimental NeuroTherapeutics*, (2004) 1:36-45 at 41.

specific details on how therapy should be conducted in the clinic. Rather, they serve to identify fundamental neural and behavioral principles of recovery that are readily observable in the laboratory and can be used to guide the development of novel clinical therapies."[18] Graham et al. echoes this conclusion of Kleim.[19]

In an article entitled "Toward Wisdom From Failure", Gladstone, D. J. et al. ("Gladstone") provides some numbers to back up the difficulty in translating animal models into clinical treatment. They state that "[a]ccording to the summary of historical trends in clinical stroke trials by Kidwell et al, the 20th century saw the publication of 178 controlled trials of acute stroke therapies in the English-language literature, yet only a few produced 'positive' results."[20] Gladstone concludes by warning that "[r]esearchers must become more cognizant of the pitfalls and paradoxes that have arisen in attempting to translate the results of animal studies into clinical trials of neuroprotective stroke therapy."[21]

Gorelick, P.B. cites "shortcomings of the experimental model" as the reason for the failure of treatment in human trials of acute ischemic stroke.[22] The statement of Gorelick was precipitated, in part, by a report by Lees, K.R. et al. appearing in the same issue of *The Lancet* detailing results of clinical trials on the glycine antagonist gavestinal.[23] Despite the reduction in infarct size in rats by slightly more than 50% when administered intravenously within 6 hours after onset of middle cerebral artery occlusion (as reported by Warner et al.), treatment with gavestinal within 6 hours of acute ischemic stroke in the clinical trial did not improve outcome.[24]

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[17] Kleim, J.A. et al. "Rat Models of Upper Extremity Impairment in Stroke" *Institute for Laboratory Animal Research Journal*, (2007) Vol. 48(4):374-384 at 375.

[18] Kleim, J.A. et al. "Rat Models of Upper Extremity Impairment in Stroke" *Institute for Laboratory Animal Research Journal* (2007) Vol. 48(4):374-384 at 375.

[19] Graham, et al, "Animal Models of Ischemic Stroke:Balancing Experimental Aims and Animal Care", Comparative Medicine, (2004) Vol. 54(5): pages 486-496, at 492: "Many animal models of ischemic stroke are available, but no model in particular fully mimics the diversity of the human clinical ischemic stroke. Nonetheless, these models are useful for studying specific injurious and protective mechanisms…"

[20] Gladstone, D. J. et al. "Toward Wisdom from Failure: Lessons From Neuroprotection Stroke Trials and New Therapeutic Directions", *Stroke* (2002) 33;2123-2136 at 2123.

[21] Gladstone, D. J. et al. "Toward Wisdom from Failure: Lessons From Neuroprotection Stroke Trials and New Therapeutic Directions", *Stroke* (2002) 33;2123-2136 at 2131.

[22] Gorelick, P.B., "Neuroprotection in acute ischemic stroke: a tale of for whom the bell tolls?", *The Lancet*, (2000) Vol. 355, page 1925-1926.

[23] Lees, K.R. et al., "Glycine antagonist (gavestinal) in neuroportection (GAIN International) in patients with acute stroke: a randomized controlled trial" *The Lancet*, (2000) Vol. 355, pages 1949-1954.

[24] Lees, K.R. et al., "Glycine antagonist (gavestinal) in neuroportection (GAIN International) in patients with acute stroke: a randomized controlled trial" *The Lancet*, (2000) Vol. 355, pages 1949-1954 at page 1949.

Drummond, J.C. et al, responding to Gorelick, suggested that failure in the clinical trials resulted from limitations of the preclinical studies in rodent models.[25]

One of the most unequivocal statements in this regard is made by the European Stoke Network. They state that "[g]iven the devastating failure rates of potential new interventions, animal models of stroke have quite rightly been questioned for their relevance."[26]

The Office asserts that "[t]he crux of the argument is that rodent models of ischemia were entirely useless in their ability to predict human therapies."[27] Applicant respectfully disagrees (objects) with this characterization of Applicants' position regarding rodent models. As indicated by Kleim in the excpert above, "animal models of stroke are not [necessarily] designed to mirror the human condition nor provide specific details on how therapy should be conducted in the clinic." The issue is whether, based upon the results of these animal models and without the benefit of hindsight, one of ordinary skill in the art would have a reasonable expectation of success in making the claimed invention based upon the combination and/or modification of the cited prior art when combined with the state of the art and the knowledge of one of skill in the art at the time of the invention. The excerpts above from the various sources would not indicate that this would be the case.

The Office goes on to state that "[w]hile rodent cerebral artery occlusion studies may well reveal false positives (therapies which are efficacious in rodents but not in humans), and may fail to reproduce every single aspect of stroke in humans, the models nonetheless are reasonable. Therapies known to be effective for treatment of stroke in humans are also effective for treatment of stroke in rodents." Two points are noteworthy here. First, the question is not whether therapies known to be effective for treatment of stroke in ***humans*** are also effective for treatment of stroke in ***rodents***. Instead, the question is whether therapies known to be effective for treatment of stroke in ***rodents*** are also effective for treatment of stroke in ***humans***. Second, if the results of the failed trials based upon positive results in rodent models may be characterized as "false positives", then false positives have been the rule rather than the exception (e.g. see Gladstone, D. J. et al., above). While the models are not "unreasonable", to borrow the Office's wording, the question is the extent to which one can take the teachings.

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[25] Drummond, J.C. et al., "Neuroprotection failure in stroke", *The Lancet*, (2000) Vol. 356, pages 1032-10330.
[26] As accessed at http://www.europeanstrokenetwork.eu/index.php?option=com_content&view=article&id=40&Itemid=49 on Nov. 12, 2008 at 12:32 PM EST.

As indicated above, "[f]or a prior-art reference, or a combination of references, to render a claimed invention obvious, one of ordinary skill in the art at the time the invention was made must have expected a reasonable chance of success in applying the teachings of the references to arrive at the claimed invention."[28] "While absolute certainty is not necessary to establish a reasonable expectation of success, there can be little better evidence negating an expectation of success than actual reports of failure." The reports detailed above outline the vast number of failures that have been seen in attempting to realize clinically relevant treatment for stroke based upon experiments conducted in rodent models of the disease. Therefore, one of ordinary skill in the art at the time the invention was made would not have expected a reasonable chance of success in applying the teachings of the references to arrive at the claimed invention. It is therefore respectfully requested that the Office withdraw the rejection of claims 1, 2, 4, and 17 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,851,832 to Weiss (the '832 patent) in view of Sanberg et al. (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9) and Grabowski (1994. Exp Neural. 127(1):126-136).

<u>Sanberg in view of the '832 Patent and Uchida:</u>

Claims 7, 10, 12-17 and 19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg (1996. Soc. Neurosci. Abstr. 22(1-3):578, abstract 232.9) in view of Weiss (U.S. Patent (5,851,832) and Uchida (1995. Exp. Neurol 132:194-208). Applicant respectfully traverses this rejection on the grounds that (1) one or more elements are missing from the cited combination and (2) that the cited art, in combination with state of the art and the knowledge of one of ordinary skill in the art at the time of the invention, would not have imbued one of ordinary skill in the art with a reasonable expectation of success. Applicant submits that the rejection is improper for reasons of record as presented above with respect to the rejection of claims 1, 2, 4, and 17 over the '832 patent in view of Sanberg and Grabowski. It is therefore respectfully requested that the Office withdraw the rejection of claims 7, 10, 12-17 and 19 under 35 U.S.C. 103(a) as being unpatentable over 7, 10, Sanberg (1996. Soc. Neurosci. Abstr. 22(1-3):578, abstract 232.9) in view of Weiss (U.S. Patent (5,851,832) and Uchida (1995. Exp. Neurol

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[27] Office action dated 14 August 2008 at page 3.

132:194-208).

[28] PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360, 83 U.S.P.Q.2d 1289, 1301–02 (Fed. Cir. 2007), cert. denied, 2008 WL 102402 (U.S. 2008).

Conclusion

For the reasons cited above, Applicant believes that claims 1-2, 4, 7, 10, 12-17 and 19 are patentable and in condition for allowance.

If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (813) 925-8505 is requested.

Very respectfully,

SMITH & HOPEN

/michael m mcgaw/

By:________________________

Dated: November 14, 2008

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CERTIFICATE OF ELECTRONIC TRANSMISSION TRANSMISSION
(37 C.F.R. 2.190(B))

I HEREBY CERTIFY that this Amendment D is being electronically transmitted to the United States Patent and Trademark Office through EFS Web on November 14, 2008.

/erica gossage/

Date: November 14, 2008

Erica Gossage